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DATE: Friday, January 02, 2004

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☐	L4	L2 and NADPH	42
☐	L3	LNADPH	0
☐	L2	L1 and (optical same assay or UV same assay or fluorescen$5)	173
☐	L1	squalene synthase or squalene synthetase or (e adj2 c adj2. adj2 5 adj2 1 adj2 21) or (fpp adj3 fpp farnesyltransferase) or (farnesyl-diphosphate farnesyltransferase)	945

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☐ 1. Document ID: US 20040002105 A1

L4: Entry 1 of 42 File: PGPB Jan 1, 2004

PGPUB-DOCUMENT-NUMBER: 20040002105
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040002105 A1

TITLE: Methods of identifying genes for the manipulation of triterpene saponins

PUBLICATION-DATE: January 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dixon, Richard A.	Ardmore	OK	US	
Achnine, Lahoucine	Ardmore	OK	US	
Suzuki, Hideyuki	Kisarazu-shi	OK	JP	
He, Xian-Zhi	Ardmore	OK	US	
Wang, Liangjiang	Ardmore		US	

US-CL-CURRENT: 435/6; 435/7.2, 800/278

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 20030188339 A1

L4: Entry 2 of 42 File: PGPB Oct 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030188339
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030188339 A1

TITLE: Regulatory sequences for regulation of gene expression in plants and other organisms, and compositions, products and methods related thereto

PUBLICATION-DATE: October 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Abdullah, Siti Nor Akmar	Kajang		MY	
Ramli, Zubaidah	Kajang		MY	

US-CL-CURRENT: 800/281; 435/193, 435/320.1, 435/419, 536/23.2, 554/9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 3. Document ID: US 20030186871 A1

L4: Entry 3 of 42 File: PGPB Oct 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030186871
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030186871 A1

TITLE: Compositions and methods for diagnosing and treating diabetes, insulin resistance and dyslipidemia

PUBLICATION-DATE: October 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Waters, Steve	San Ramon	CA	US	
Moodie, Shonna	San Francisco	CA	US	
Lavan, Brian	San Francisco	CA	US	
Gustafson, Thomas A.	Danville	CA	US	

US-CL-CURRENT: 514/12; 435/6, 435/7.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 4. Document ID: US 20030162829 A1

L4: Entry 4 of 42 File: PGPB Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030162829
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030162829 A1

TITLE: Combination of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-a (HMG-CoA) reductase inhibitor

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kindness, George	Middletown	OH	US	
Schumm, Brooke III	Ellicott City	MD	US	
Guilford, F. Timothy	Palo Alto	CA	US	

US-CL-CURRENT: 514/473; 514/460, 514/548, 514/562

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 5. Document ID: US 20030157583 A1

L4: Entry 5 of 42 File: PGPB Aug 21, 2003

PGPUB-DOCUMENT-NUMBER: 20030157583
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030157583 A1

TITLE: Methods for determining squalene synthase activity

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Stevens, Donna	Hillsborough	NC	US	
Wang, Xiao-Zhuo	East Lyme	CT	US	
Rice, John	Pittsboro	NC	US	
Nye, Beth	Morrisville	NC	US	
Broadwell, David	Garner	NC	US	
Glassbrook, Norman	Chapel Hill	NC	US	
Sevala, Veeresh	Cary	NC	US	
Crawford, John	Raleigh	NC	US	
Stewart, Sandy	Durham	NC	US	

US-CL-CURRENT: 435/15; 435/189, 435/193, 435/25, 435/320.1, 435/419, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 6. Document ID: US 20030143700 A1

L4: Entry 6 of 42 File: PGPB Jul 31, 2003

PGPUB-DOCUMENT-NUMBER: 20030143700
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030143700 A1

TITLE: Methods for producing optically active alcohols

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yamamoto, Hiroaki	Ibaraki		JP	
Ueda, Momoko	Ibaraki		JP	
Pan, Ritsuzui	Niigata		JP	
Hamatani, Takeshi	Niigata		JP	

US-CL-CURRENT: 435/120; 435/155

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 7. Document ID: US 20030134301 A1

L4: Entry 7 of 42 File: PGPB Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030134301
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030134301 A1

TITLE: Identification and use of molecules implicated in pain

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brooksbank, Robert Alan	Cambridge	MI	GB	
Dixon, Alistair Kerr	Cambridge		GB	
Lee, Kevin	Cambridge		GB	
Pinnock, Robert Denham	Ann Arbor		US	

US-CL-CURRENT: 435/6; 435/194, 435/7.1, 435/7.21, 800/3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 8. Document ID: US 20030093226 A1

L4: Entry 8 of 42 File: PGPB May 15, 2003

PGPUB-DOCUMENT-NUMBER: 20030093226
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030093226 A1

TITLE: Methods for the identification of reporter and target molecules using comprehensive gene expression profiles

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ashby, Matthew	Mill Valley	CA	US	
Scherer, Stewart	Moraga	CA	US	
Phillips, John W.	Kirkland	WA	US	
Ziman, Michael	Seattle	WA	US	
Marini, Nicholas	San Francisco	CA	US	

US-CL-CURRENT: 702/20; 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 9. Document ID: US 20030082511 A1

L4: Entry 9 of 42 File: PGPB May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030082511
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030082511 A1

TITLE: Identification of modulatory molecules using inducible promoters

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brown, Steven J.	San Diego	CA	US	
Dunnington, Damien J.	San Diego	CA	US	
Clark, Imran	San Diego	CA	US	

US-CL-CURRENT: 435/4; 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 10. Document ID: US 20030017167 A1

L4: Entry 10 of 42 File: PGPB Jan 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030017167
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030017167 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	

US-CL-CURRENT: 424/185.1; 435/320.1, 435/325, 435/6, 435/69.1, 435/7.23, 514/44, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 11. Document ID: US 20020169195 A1

L4: Entry 11 of 42 File: PGPB Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020169195
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020169195 A1

TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and an HMG-CoA inhibitor and cystine to enhance glutathione

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kindness, George	Middletown	OH	US	
Schumm, Brooke III	Ellicott City	MD	US	
Guilford, F. Timothy	Palo Alto	CA	US	

US-CL-CURRENT: 514/406; 514/562

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 12. Document ID: US 20020132781 A1

L4: Entry 12 of 42 File: PGPB Sep 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020132781
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020132781 A1

TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and A 3-hydroxy-3-methylglutaryl-coenzyme-A (HMG-CoA) reductase inhibitor

PUBLICATION-DATE: September 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kindness, George	Middletown	OH	US	
Schumm, Brooke III	Ellicott City	MD	US	
Guilford, F. Timothy	Palo Alto	CA	US	

US-CL-CURRENT: 514/27; 514/100, 514/406, 514/423, 514/456, 514/460, 514/547

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 13. Document ID: US 20020120013 A1

L4: Entry 13 of 42 File: PGPB Aug 29, 2002

PGPUB-DOCUMENT-NUMBER: 20020120013
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020120013 A1

TITLE: Regulation of phospholipase D activity

PUBLICATION-DATE: August 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Serhan, Charles N.	Needham	MA	US	

US-CL-CURRENT: 514/712; 514/520, 514/720

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 14. Document ID: US 20020107289 A1

L4: Entry 14 of 42 File: PGPB Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020107289
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020107289 A1

TITLE: Regulation of phospholipase D activity

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Serhan, Charles N.	Needham	MA	US	

US-CL-CURRENT: 514/560; 514/521

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 15. Document ID: US 20020094549 A1

L4: Entry 15 of 42 File: PGPB Jul 18, 2002

PGPUB-DOCUMENT-NUMBER: 20020094549
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020094549 A1

TITLE: Screening methods for presqualene diphosphate analogs

PUBLICATION-DATE: July 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Serhan, Charles N.	Needham	MA	US	
Levy, Bruce D.	West Roxbury	MA	US	

US-CL-CURRENT: 435/19; 435/25

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 16. Document ID: US 20020086894 A1

L4: Entry 16 of 42 File: PGPB Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020086894
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020086894 A1

TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-a (HMG-CoA) reductase inhibitor

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kindness, George	Middletown	OH	US	
Schumm, Brooke III	Ellicott City	MD	US	
Guilford, F. Timothy	Palo Alto	CA	US	

US-CL-CURRENT: 514/403; 514/460, 514/548, 514/562

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 17. Document ID: US 20020040127 A1

L4: Entry 17 of 42 File: PGPB Apr 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020040127
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020040127 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Hepler, William T.	Seattle	WA	US	
Clapper, Jonathan D.	Seattle	WA	US	
Wang, Aijun	Issaquah	WA	US	
Secrist, Heather	Seattle	WA	US	

US-CL-CURRENT: 530/350; 435/320.1, 435/325, 435/69.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 18. Document ID: US 20020023281 A1

L4: Entry 18 of 42 File: PGPB Feb 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020023281
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020023281 A1

TITLE: Expressed sequences of arabidopsis thaliana

PUBLICATION-DATE: February 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gorlach, Jorn	Durham	NC	US	
An, Yong-Qiang	San Diego	CA	US	
Hamilton, Carol M.	Apex	NC	US	
Price, Jennifer L.	Raleigh	NC	US	
Raines, Tracy M.	Durham	NC	US	
Yu, Yang	Martinsville	NJ	US	
Rameaka, Joshua G.	Durham	NC	US	
Page, Amy	Durham	NC	US	
Mathew, Abraham V.	Cary	NC	US	
Ledford, Brooke L.	Holly Springs	NC	US	
Woessner, Jeffrey P.	Hillsborough	NC	US	
Haas, William David	Durham	NC	US	
Garcia, Carlos A.	Carrboro	NC	US	
Kricker, Maja	Pittsboro	NC	US	
Slater, Ted	Apex	NC	US	
Davis, Keith R.	Durham	NC	US	
Allen, Keith	Cary	NC	US	
Hoffman, Neil	Chapel Hill	NC	US	
Hurban, Patrick	Raleigh	NC	US	

US-CL-CURRENT: 800/288; 435/4, 536/23.2, 536/23.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 19. Document ID: US 20010051335 A1

L4: Entry 19 of 42 File: PGPB Dec 13, 2001

PGPUB-DOCUMENT-NUMBER: 20010051335
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010051335 A1

TITLE: POLYNUCLEOTIDES AND POLYPEPTIDES DERIVED FROM CORN TASSEL

PUBLICATION-DATE: December 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
LALGUDI, RAGHUNATH V.	CLAYTON	MO	US	
ITO, LAURA Y.	PLEASANTON	CA	US	
SHERMAN, BRADLEY K.	OAKLAND	CA	US	

US-CL-CURRENT: 435/6; 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 20. Document ID: US 20010001062 A1

L4: Entry 20 of 42 File: PGPB May 10, 2001

PGPUB-DOCUMENT-NUMBER: 20010001062
PGPUB-FILING-TYPE: new-utility
DOCUMENT-IDENTIFIER: US 20010001062 A1

TITLE: Screening methods for presqualene diphosphate analogs

PUBLICATION-DATE: May 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Serhan, Charles N.	Wellesley	MA	US	
Levy, Bruce D.	West Roxbury	MA	US	

US-CL-CURRENT: 435/25; 435/21

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 21. Document ID: US 6630617 B1

L4: Entry 21 of 42 File: USPT Oct 7, 2003

US-PAT-NO: 6630617
DOCUMENT-IDENTIFIER: US 6630617 B1

TITLE: Enzymes involved in squalene metabolism

DATE-ISSUED: October 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Famodu; Omolayo O.	Newark	DE		
Kinney; Anthony J.	Wilmington	DE		
Rafalski; J. Antoni	Wilmington	DE		

US-CL-CURRENT: 800/298; 435/419, 435/468, 536/23.6, 800/278

ABSTRACT:

This invention relates to an isolated nucleic acid fragment encoding a squalene metabolic enzyme. The invention also relates to the construction of a chimeric gene encoding all or a portion of the squalene metabolic enzyme, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of the squalene metabolic enzyme in a transformed host cell.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 1,7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 22. Document ID: US 6607879 B1

L4: Entry 22 of 42 File: USPT Aug 19, 2003

US-PAT-NO: 6607879
DOCUMENT-IDENTIFIER: US 6607879 B1

TITLE: Compositions for the detection of blood cell and immunological response gene expression

DATE-ISSUED: August 19, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cocks; Benjamin G.	Sunnyvale	CA		
Stuart; Susan G.	Montara	CA		
Seilhamer; Jeffrey J.	Los Altos Hills	CA		

US-CL-CURRENT: 435/6; 435/69.1, 536/23.1, 536/24.1, 536/24.3, 536/24.31, 536/24.32, 536/24.33

ABSTRACT:

The present invention relates to a composition comprising a plurality of polynucleotide probes. The composition can be used as hybridizable array elements in a microarray. The present invention also relates to a method for selecting polynucleotide probes for the composition.

7 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

☐ 23. Document ID: US 6534540 B2

L4: Entry 23 of 42 File: USPT Mar 18, 2003

US-PAT-NO: 6534540
DOCUMENT-IDENTIFIER: US 6534540 B2

TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-a (HMG-CoA) reductase inhibitor

DATE-ISSUED: March 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kindness; George	Middletown	OH	45044	
Schumm, III; Brooke	Ellicott City	MD	21042	
Guilford; F. Timothy	Palo Alto	CA	94301	

US-CL-CURRENT: 514/461; 514/473

ABSTRACT:

The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer especially prostate cancer and a method of treatment of cancer by that combination, especially prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compound, particularly cystine, for the treatment of cancer especially

prostate cancer and a method of treatment of cancer by that combination, especially prostate cancer. Based on the clinical results of retardation, but not cure of cancer, the combination has the characteristic of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer.

11 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

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☐ 24. Document ID: US 6416965 B2

L4: Entry 24 of 42 File: USPT Jul 9, 2002

US-PAT-NO: 6416965
DOCUMENT-IDENTIFIER: US 6416965 B2

TITLE: Screening methods for presqualene disphosphate analogs

DATE-ISSUED: July 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Serhan; Charles N.	Wellesley	MA		
Levy; Bruce D.	West Roxbury	MA		

US-CL-CURRENT: 435/18; 435/25

ABSTRACT:

The present invention is directed to presqualene diphosphate (PSDP) analogs having an active region of natural PSDP and a metabolic transformation region resistant to rapid intracellular inactivation in vivo. For example, PSDP and its stable analogs can inhibit neutrophil signal transduction events in cellular activation that result in the generation of active oxygen species, regulation of leukocyte adherence, both homotypic (leukocyte--leukocyte) or heterotypic adherence with leukocytes and epithelial cells of mucosal origin or endothelial cells of vascular origin. These analogs can also be used to regulate leukocyte-dependent tissue injury.

12 Claims, 25 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

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☐ 25. Document ID: US 6353026 B1

L4: Entry 25 of 42 File: USPT Mar 5, 2002

US-PAT-NO: 6353026

DOCUMENT-IDENTIFIER: US 6353026 B1

TITLE: Regulation of phospholipase D activity

DATE-ISSUED: March 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Serhan; Charles N.	Wellesley	MA		

US-CL-CURRENT: 514/560; 514/558

ABSTRACT:

Novel inhibitors of polyisoprenyl phosphate signaling regulates phopholipase D activity.

16 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 26. Document ID: US 6284910 B1

L4: Entry 26 of 42 File: USPT Sep 4, 2001

US-PAT-NO: 6284910
DOCUMENT-IDENTIFIER: US 6284910 B1

TITLE: Farnesyl pyrophosphate analogs

DATE-ISSUED: September 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Spielmann; Hans Peter	Lexington	KY		
Andres; Douglas A.	Lexington	KY		
Chehade; Kareem A. H.	Lexington	KY		

US-CL-CURRENT: 558/152; 560/20

ABSTRACT:

The post-translational addition of a farnesyl moiety to the Ras oncoprotein is essential for its membrane localization and is required for both its biological activity and ability to induce malignant transformation. The present invention describes design and synthesis of a farnesylpyrophosphate (FPP) analog, 8-anilinogeranyl pyrophosphate (AGPP) that is transferred to Ras by farnesyltransferase (FTase), in which the .omega.-terminal isoprene unit of the farnesyl group has been replaced with an aniline functionality. AGPP potently inhibited FTase activity in vitro (IC.sub.50 =0.6 .mu.M) and is highly selective

showing little inhibitory activity against either geranylgeranyl-protein transferase type I (GGTase I) (IC.sub.50 =31 .mu.M) or the utilization of FPP by the enzyme squalene synthase (IC.sub.50 =1000 .mu.M). Kinetic analyses suggest that AGPP acts as a competitive inhibitor of FTase with respect to FPP. In vitro studies using [.sup.3 H]AGPP show that the analog was appropriately transferred by FTase to Ras. Derivitization of AGPP with a bulky iodo group on the aniline ring does not significantly alter its biochemical properties. These data indicate that the modified molecules are the first truly transferable analogs of FPP and open the door to additional analogs to probe the biological function of protein farnesylation.

17 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

☐ 27. Document ID: US 6251622 B1

L4: Entry 27 of 42 File: USPT Jun 26, 2001

US-PAT-NO: 6251622
DOCUMENT-IDENTIFIER: US 6251622 B1

TITLE: Screening methods for presqualene diphosphate analogs

DATE-ISSUED: June 26, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Serhan; Charles N.	Wellesley	MA		
Levy; Bruce D.	West Roxbury	MA		

US-CL-CURRENT: 435/18; 435/25

ABSTRACT:

The present invention is directed to presqualene diphosphate (PSDP) analogs having an active region of natural PSDP and a metabolic transformation region resistant to rapid intracellular inactivation in vivo. For example, PSDP and its stable analogs can inhibit neutrophil signal transduction events in cellular activation that result in the generation of active oxygen species, regulation of leukocyte adherence, both homotypic (leukocyte-leukocyte) or heterotypic adherence with leukocytes and epithelial cells of mucosal origin or endothelial cells of vascular origin. These analogs can also be used to regulate leukocyte-dependent tissue injury.

8 Claims, 25 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

☐ 28. Document ID: US 6066466 A

L4: Entry 28 of 42 File: USPT May 23, 2000

US-PAT-NO: 6066466
DOCUMENT-IDENTIFIER: US 6066466 A

TITLE: Screening methods for presqualene diphosphate analogs

DATE-ISSUED: May 23, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Serhan; Charles N.	Wellesley	MA		
Levy; Bruce D.	West Roxbury	MA		

US-CL-CURRENT: 435/18; 435/25

ABSTRACT:

The present invention is directed to presqualene diphosphate (PSDP) analogs having an active region of natural PSDP and a metabolic transformation region resistant to rapid intracellular inactivation in vivo. For example, PSDP and its stable analogs can inhibit neutrophil signal transduction events in cellular activation that result in the generation of active oxygen species, regulation of leukocyte adherence, both homotypic (leukocyte-leukocyte) or heterotypic adherence with leukocytes and epithelial cells of mucosal origin or endothelial cells of vascular origin. These analogs can also be used to regulate leukocyte-dependent tissue injury.

5 Claims, 25 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw. D

☐ 29. Document ID: US 6008205 A

L4: Entry 29 of 42 File: USPT Dec 28, 1999

US-PAT-NO: 6008205
DOCUMENT-IDENTIFIER: US 6008205 A

TITLE: Polyisoprenyl phosphate stable analogs for regulation of neutrophil responses

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Serhan; Charles N.	Wellesley	MA
Levy; Bruce D.	West Roxbury	MA

US-CL-CURRENT: 514/102; 514/106, 514/107, 514/108, 558/152, 558/155

ABSTRACT:

The present invention is directed to presqualene diphosphate (PSDP) analogs having an active region of natural PSDP and a metabolic transformation region resistant to rapid intracellular inactivation in vivo. For example, PSDP and its stable analogs can inhibit neutrophil signal transduction events in cellular activation that result in the generation of active oxygen species, regulation of leukocyte adherence, both homotypic (leukocyte-leukocyte) or heterotypic adherence with leukocytes and epithelial cells of mucosal origin or endothelial cells of vascular origin. These analogs can also be used to regulate leukocyte-dependent tissue injury.

6 Claims, 21 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

☐ 30. Document ID: US 5861496 A

L4: Entry 30 of 42 File: USPT Jan 19, 1999

US-PAT-NO: 5861496
DOCUMENT-IDENTIFIER: US 5861496 A

TITLE: Human squalene epoxidase

DATE-ISSUED: January 19, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hillman; Jennifer L.	San Jose	CA		
Hawkins; Phillip R.	Mountain View	CA		

US-CL-CURRENT: 536/23.2; 435/189, 435/252.3, 435/320.1, 435/69.1, 536/24.3

ABSTRACT:

The present invention provides a human squalene epoxidase (HSQEP) and polynucleotides which identify and encode HSQEP. The invention also provides genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding HSQEP and a method for producing HSQEP. The invention also provides for the use of HSQEP and agonists, antibodies, or antagonists specifically binding HSQEP, in the prevention and treatment of diseases associated with expression of HSQEP. Additionally, the invention provides for the use of antisense molecules to polynucleotides encoding HSQEP for the treatment of diseases associated with the expression of HSQEP. The invention also provides diagnostic assays which utilize the polynucleotide, or fragments or the complement thereof,

and antibodies specifically binding HSQEP.

3 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

☐ 31. Document ID: US 5589372 A

L4: Entry 31 of 42 File: USPT Dec 31, 1996

US-PAT-NO: 5589372
DOCUMENT-IDENTIFIER: US 5589372 A

TITLE: Squalene synthetase

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Robinson; Gordon W.	Lawrenceville	NJ		

US-CL-CURRENT: 435/193; 435/252.3, 435/254.11, 435/320.1, 435/348, 435/355, 435/358, 435/365, 536/23.2, 536/24.3

ABSTRACT:

Nucleic acid sequences, particularly DNA sequences, coding for all or part of a squalene synthetase, expression vectors containing the DNA sequences, host cells containing the expression vectors, and methods utilizing these materials. The invention also concerns polypeptide molecules comprising all or part of a squalene synthetase, and methods for producing these polypeptide molecules.

20 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 12

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

☐ 32. Document ID: US 5362752 A

L4: Entry 32 of 42 File: USPT Nov 8, 1994

US-PAT-NO: 5362752
DOCUMENT-IDENTIFIER: US 5362752 A

TITLE: Chemical compounds

DATE-ISSUED: November 8, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Arison; Byron H.	Watchung	NJ		
Berger; Gregory D.	Belle Mead	NJ		
Huang; Leeyuan	Watchung	NJ		
MacConnell; John G.	Westfield	NJ		

US-CL-CURRENT: 514/533; 549/228, 549/229, 549/270, 549/271, 549/285, 549/292, 549/305, 549/318, 549/328, 554/116

ABSTRACT:

New cholesterol lowering compounds are formed from the photochemical treatment of zaragozic acid A.

8 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. D

☐ 33. Document ID: US 5359096 A

L4: Entry 33 of 42 File: USPT Oct 25, 1994

US-PAT-NO: 5359096
DOCUMENT-IDENTIFIER: US 5359096 A

TITLE: Cholesterol lowering compounds

DATE-ISSUED: October 25, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Treiber; Laszlo R.	Gillette	NJ		
Arison; Byron H.	Watchung	NJ		
Chen; Shieh-Shung T.	Morganville	NJ		
Doss; George A.	Westfield	NJ		
Huang; Leeyuan	Watchung	NJ		
MacConnell; John G.	Westfield	NJ		

US-CL-CURRENT: 549/363

ABSTRACT:

New cholesterol lowering compounds are formed from the photochemical treatment of the zaragozic acids.

26 Claims, 0 Drawing figures
Exemplary Claim Number: 13

☐ 34. Document ID: US 5322855 A

L4: Entry 34 of 42 File: USPT Jun 21, 1994

US-PAT-NO: 5322855
DOCUMENT-IDENTIFIER: US 5322855 A

TITLE: Cholesterol lowering compounds

DATE-ISSUED: June 21, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Treiber; Laszlo R.	Gillette	NJ		
Doss, George A.	Westfield	NJ		
Arison; Byron H.	Watchung	NJ		

US-CL-CURRENT: 514/452; 549/363

ABSTRACT:

Zaragozic acids isolated from a culture of MF5465 have been subjected to photoreaction, then derivatized at the 4-keto position. The resulting derivatives are active as squalene synthetase inhibitors and are useful in the treatment of hypercholesterolemia.

5 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Drawi De

☐ 35. Document ID: US 5317031 A

L4: Entry 35 of 42 File: USPT May 31, 1994

US-PAT-NO: 5317031
DOCUMENT-IDENTIFIER: US 5317031 A

TITLE: Cholesterol lowering compounds

DATE-ISSUED: May 31, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
MacConnell; John G.	Watchung	NJ		
Arison; Byron H.	Watchung	NJ		
Doss; George A.	Westfield	NJ		

Monaghan; Richard L. Somerset NJ

US-CL-CURRENT: 514/452

ABSTRACT:

Cholesterol lowering compounds and compositions are formed from the photochemical treatment of the Zaragozic Acids followed by esterification. These compounds and compositions are active squalene synthetase inhibitors useful in the treatment of hypercholesterolemia.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw. D

☐ 36. Document ID: US 5270332 A

L4: Entry 36 of 42 File: USPT Dec 14, 1993

US-PAT-NO: 5270332
DOCUMENT-IDENTIFIER: US 5270332 A

TITLE: Cholesteral lowering agents

DATE-ISSUED: December 14, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chen; Shieh-Shung T.	Morganville	NJ		
Huang; Leeyuan	Watchung	NJ		
MacConnell; John G.	Westfield	NJ		
Polishook; Jon D.	Scotch Plains	NJ		
White; Raymond F.	Englishtown	NJ		

US-CL-CURRENT: 514/452; 549/363

ABSTRACT:

This invention relates to compounds of structural formula (I): ##STR1## which are squalene synthase inhibitors and thus useful as cholesterol lowering agents. The compounds also exhibit antifungal activity and are inhibitors of farnesyl-protein transferase.

7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw. D

☐ 37. Document ID: US 5254727 A

L4: Entry 37 of 42 File: USPT Oct 19, 1993

US-PAT-NO: 5254727
DOCUMENT-IDENTIFIER: US 5254727 A

TITLE: Acyclic tricarboxylic acid compounds

DATE-ISSUED: October 19, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dufresne; Claude	East Brunswick	NJ		
Jones; E. Tracy T.	Solana Beach	CA		
Ferrell; Leslie A.	Cranford	NJ		

US-CL-CURRENT: 562/470; 560/60

ABSTRACT:

Two acyclic tricarboxylic acid compounds have been isolated from the fermentation of Sporormiella intermedia. The compounds and their derivatives may be used as antifungal agents, cholesterol lowering agents and as anticancer agents.

8 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 38. Document ID: US 5132320 A

L4: Entry 38 of 42 File: USPT Jul 21, 1992

US-PAT-NO: 5132320
DOCUMENT-IDENTIFIER: US 5132320 A

TITLE: Squalene synthetase inhibitors

DATE-ISSUED: July 21, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bergstrom; James D.	Neshanic	NJ		
Hensens; Otto D.	Red Bank	NJ		
Dufresne; Claude	Edison	NJ		
Huang; Leeyuan	Watchung	NJ		
Onishi; Janet C.	Mountainside	NJ		
Zink; Deborah L.	Manalapan	NJ		

US-CL-CURRENT: 514/452; 549/363

ABSTRACT:

This invention relates to compounds of structural formula (I): ##STR1## which are squalene synthetase inhibitors and thus useful as cholesterol lowering agents.

14 Claims, 2 Drawing figures
Exemplary Claim Number: 1,11
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 39. Document ID: US 5096923 A

L4: Entry 39 of 42 File: USPT Mar 17, 1992

US-PAT-NO: 5096923
DOCUMENT-IDENTIFIER: US 5096923 A

TITLE: Novel squalene synthetase inhibitors

DATE-ISSUED: March 17, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bergstrom; James D.	Neshanic	NJ		
Hensens; Otto D.	Red Bank	NJ		
Huang; Leeyuan	Watchung	NJ		
Liesch; Jerrold M.	Princeton Junction	NJ		
Onishi; Janet C.	Mountainside	NJ		
Vanmiddlesworth; Frank L.	Fanwood	NJ		

US-CL-CURRENT: 514/452; 549/363

ABSTRACT:

This invention relates to compounds of structural formula (I): ##STR1## which are squalene synthetase inhibitors and thus useful as cholesterol lowering agents.

14 Claims, 2 Drawing figures
Exemplary Claim Number: 1,11
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 40. Document ID: US 5055487 A

L4: Entry 40 of 42 File: USPT Oct 8, 1991

US-PAT-NO: 5055487
DOCUMENT-IDENTIFIER: US 5055487 A

TITLE: Novel anti-fungal compounds

DATE-ISSUED: October 8, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bartizal; Kenneth F.	Somerset	NJ		
Milligan; James A.	Robbinsville	NJ		
Rozdilsky; Walter	Cliffwood Beach	NJ		
Onishi; Janet C.	Mountainside	NJ		

US-CL-CURRENT: 514/452

ABSTRACT:

This invention relates to a method of inhibiting fungal growth by employing an antifungal amount of a compound of formula (I): ##STR1##

6 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Terms	Documents
L2 and NADPH	42

```
=> file .nash
=> s squalene synthetase or squalene synthase or e (2w) C (2w) 2.5.1.21 or farnesyl-diphosphate
farnesyltransferase or fpp:fpp farnesyltransferase
L1          326 FILE MEDLINE
L2          789 FILE CAPLUS
L3          622 FILE SCISEARCH
L4          135 FILE LIFESCI
L5          521 FILE BIOSIS
L6          446 FILE EMBASE

TOTAL FOR ALL FILES
L7         2839 SQUALENE SYNTHETASE OR SQUALENE SYNTHASE OR E (2W) C (2W) 2.5.1.
                21 OR FARNESYL-DIPHOSPHATE FARNESYLTRANSFERASE OR FPP:FPP FARNES
                YLTRANSFERASE

=> s l7 and (assay or activity)
TOTAL FOR ALL FILES
L14        1303 L7 AND (ASSAY OR ACTIVITY)

=> s l7 and assay


TOTAL FOR ALL FILES
L21         205 L7 AND ASSAY

=> s l21 not 2002-2004/py
TOTAL FOR ALL FILES
L28         184 L21 NOT 2002-2004/PY

=> dup rem l28
PROCESSING COMPLETED FOR L28
L29          85 DUP REM L28 (99 DUPLICATES REMOVED)

=> s l28 and fluorescen?

TOTAL FOR ALL FILES
L36           7 L28 AND FLUORESCEN?

=> dup rem l36
PROCESSING COMPLETED FOR L36
L37           3 DUP REM L36 (4 DUPLICATES REMOVED)

=> d ibib abs 1-3

L37  ANSWER 1 OF 3  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER:   2002:220603  BIOSIS
DOCUMENT NUMBER:    PREV200200220603
TITLE:              Cytotoxicity of mevastatin and other cholesterol modulators
                    in acute myeloid leukemia.
AUTHOR(S):          Li, Henry Y. [Reprint author]; Stirewalt, Derek L. [Reprint
                    author]; Willman, Cheryl L.; Appelbaum, Frederick R.
                    [Reprint author]; Zager, Richard A. [Reprint author];
                    Banker, Deborah E. [Reprint author]
CORPORATE SOURCE:   Clinical Research Division, Fred Hutchinson Cancer Research
                    Center, Seattle, WA, USA
SOURCE:             Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp.
                    714a. print.
                    Meeting Info.: 43rd Annual Meeting of the American Society
                    of Hematology, Part 1. Orlando, Florida, USA. December
                    07-11, 2001. American Society of Hematology.
                    CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE:      Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 3 Apr 2002
                    Last Updated on STN: 3 Apr 2002
AB   The mevalonate biochemical pathway produces many substances necessary for
     cell viability, including sterols essential for membrane structure and
     steroid synthesis, ubiquinones needed for mitochondrial electron
```

transport, retinoids involved in cell differentiation, and isoprenoids vital to the function of many membrane proteins. 3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase is the first rate-limiting enzyme in the mevalonate pathway, and since cholesterol is a product of this pathway, HMG-CoA reductase inhibitors (statins) are now widely used to treat hypercholesterolemia. Statins have also been shown to be selectively toxic to some tumors, including acute myeloid leukemia (AML). This toxicity has generally been attributed to their inhibition of isoprenoid production and the consequent inability of cells to prenylate proteins such as Ras and Rho. Using mevastatin as a prototypical statin, we examined the potential role of ras mutations in statin sensitivity by performing single-strand DNA conformation polymorphism analyses to interrogate both AML cell lines and primary AML cells for "hotspot" K-ras and N-ras mutations and by using Western blot **assays** to assess Ras protein characteristics. We found, however, that although mevastatin did reduce Ras protein modification and membrane localization in statin-sensitive AML cell lines with activating ras mutations, statin-sensitive primary AML cells did not necessarily carry ras mutations or over-express Ras protein. These cells also did not consistently demonstrate G1 cell cycle arrests or show the cyclin E and p27 responses associated with Rho inhibition in other statin models. In prior studies, though, we have shown that renal tubule cells increase membrane cholesterol pools in response to hypoxic and oxidant injuries and that mevastatin can sensitize these cells to injury. To determine whether cholesterol responses are similarly protective in AML and whether cholesterol reduction could contribute to the selective toxicity of statins in AML, we treated AML cell lines (HL60, KG1a, NB4, ML1) with mevastatin, zaragozic acid (an inhibitor of **squalene synthase**, the mevalonate pathway enzyme regulating cholesterol, but not isoprenoid, synthesis), or cholesterol modulators that chemically modify membrane cholesterol (including cholesterol oxidase, methylcyclodextrin, and cholesterol esterase). These treatments decreased cell cholesterol content by as much as 48%, as measured by gas chromatography and a **fluorescent** enzymatic **assay**. They were all toxic in AML cells as well, with NB4 cells demonstrating the highest sensitivity. This suggests that cholesterol reduction per se can kill AML cells. In addition, we found that cell cholesterol content rose markedly after exposure of AML cells to radiation or chemotherapy (cytarabine and daunorubicin), suggesting that cholesterol up-regulation is a stress response; the largest increase (>100%) occurred in the most statin-sensitive cell line (NB4). Co-treatment of these cells with cytarabine and either mevastatin or zaragozic acid resulted in apparently supra-additive toxicity, suggesting sensitization of cells to chemotherapy. Since zaragozic acid does not affect isoprenoid synthesis, these data suggest that cholesterol modulation may be one of the mechanisms by which mevastatin exerts its toxic effects on AML cells and that other cholesterol modulators may improve therapeutic ratios in AML by directly affecting cholesterol-dependent cytoresistance.

L37 ANSWER 2 OF 3 EMBASE
on STN

ACCESSION NUMBER: 1998382432 EMBASE
TITLE: H-Ras peptide and protein substrates bind protein farnesyltransferase as an ionized thiolate.
AUTHOR: Hightower K.E.; Huang C.-C.; Casey P.J.; Fierke C.A.
CORPORATE SOURCE: C.A. Fierke, Department of Biochemistry, Box 3711, Duke University Medical Center, Durham, NC 27710, United States. fierke@biochem.duke.edu
SOURCE: Biochemistry, (3 Nov 1998) 37/44 (15555-15562).
Refs: 74
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The zinc metalloenzyme protein farnesyltransferase (FTase) catalyzes the alkylation of a cysteine residue of protein substrates with a 15 carbon farnesyl group. We have developed **fluorescence assays** to directly measure the affinity of the enzyme for peptide and protein (Ras) substrates. A peptide corresponding to the carboxyl terminus of

H-Ras binds to FTase in the .mu.M range (K(D) = 4 .mu.M) at physiological pH; however, the peptide affinity is enhanced approximately 70-fold in a ternary complex with an enzyme-bound farnesyl diphosphate (FPP) analogue, indicating that the two substrates bind synergistically. The pH dependence of substrate binding was also investigated, and two ionizations were observed: for the ternary complex, the pK(a) values are 8.1, reflecting ionization of the thiol of the free peptide, and 6.4. The pH dependence of the ligand-metal charge-transfer band in the optical absorption spectra of a Co2+-substituted FTase ternary complex suggests that a metal-coordinated thiol ionizes with a pK(a) of 6.3. These data indicate that metal coordination of the peptide sulfur with the zinc ion in FTase lowers the pK(a) of the thiol resulting in formation of a bound thiolate at physiological pH.

L37 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 92406728 MEDLINE
DOCUMENT NUMBER: 92406728 PubMed ID: 1526971
TITLE: **Squalene synthase**-deficient mutant of Chinese hamster ovary cells.
AUTHOR: Bradfute D L; Silva C J; Simoni R D
CORPORATE SOURCE: Department of Biological Sciences, Stanford University, California 94305-5020.
CONTRACT NUMBER: GM07276 (NIGMS)
HL26502 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Sep 15) 267 (26) 18308-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19921106
Last Updated on STN: 19921106
Entered Medline: 19921019

AB **Squalene synthase** (farnesyldiphosphate:farnesyldiphosphate farnesyltransferase, EC 2.5.1.21) converts farnesyl pyrophosphate to squalene, the first metabolic step committed solely to the biosynthesis of sterols. Using a **fluorescence**-activated cell sorting technique designed to screen for cells defective in the regulated degradation of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, we isolated a **squalene synthase**-deficient mutant of Chinese hamster ovary cells. The mutant cell line, designated SSD, exhibits less than 7% of the **squalene synthase** activity of the parental cell line, CHO-HMGal. Both the SSD and the parental cells stably express HMGal, a model protein for studying the regulated degradation of HMG-CoA reductase, which consists of the membrane domain of HMG-CoA reductase fused to bacterial beta-galactosidase (Skalnik, D. G., Narita, H., Kent, C., and Simoni, R. D. (1988) J. Biol. Chem. 263, 6836-6841). In this study, the regulatory effects of mevalonate and compactin on the activity levels of HMGal are substantially reduced in SSD cells as compared to the parental cell line. In lipid-poor medium, SSD cell growth is arrested. The rate of [3H]acetate incorporation into cholesterol for the mutant SSD cells is less than 2% of the rate for the parental cells. However, the incorporation of [3H] squalene into sterols is essentially wild type for SSD cells. When the mutant SSD cells are fed [3H]acetate, radioactivity accumulates in farnesol, much of which is secreted into the medium. By growing SSD cells in lipid-poor medium, a revertant cell type, designated SSR, was isolated. In every **assay** performed the revertant SSR cells exhibited a phenotype that was essentially wild type, demonstrating that the SSD mutant phenotype was the result of a single mutation.

=> s l28 and (ultra viol? or visible light)
TOTAL FOR ALL FILES
L58 0 L28 AND (ULTRA VIOL? OR VISIBLE LIGHT)

=> s l28 and uv

TOTAL FOR ALL FILES
L65 0 L28 AND UV

```
=> s l7 and (fluorescen? or uv)
TOTAL FOR ALL FILES
L72         44 L7 AND (FLUORESCEN? OR UV)

=> s l72 not 2002-2004/py
TOTAL FOR ALL FILES
L79         32 L72 NOT 2002-2004/PY

=> dup rem l79
PROCESSING COMPLETED FOR L79
L80         15 DUP REM L79 (17 DUPLICATES REMOVED)

=> d ibib abs

L80  ANSWER 1 OF 15     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2001210199     MEDLINE
DOCUMENT NUMBER:    21195250   PubMed ID: 11298754
TITLE:              A subfraction of the yeast endoplasmic reticulum associates
                    with the plasma membrane and has a high capacity to
                    synthesize lipids.
AUTHOR:             Pichler H; Gaigg B; Hrastnik C; Achleitner G; Kohlwein S D;
                    Zellnig G; Perktold A; Daum G
CORPORATE SOURCE:   Institut fur Biochemie, Technische Universitat, and SFB
                    Biomembrane Research Center, Graz, Austria.
SOURCE:             EUROPEAN JOURNAL OF BIOCHEMISTRY, (2001 Apr) 268 (8)
                    2351-61.
                    Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY:       Germany: Germany, Federal Republic of
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200105
ENTRY DATE:         Entered STN: 20010604
                    Last Updated on STN: 20010604
                    Entered Medline: 20010531
AB   Large parts of the endoplasmic reticulum of the yeast, Saccharomyces
     cerevisiae, are located close to intracellular organelles, i.e.
     mitochondria and the plasma membrane, as shown by fluorescence
     and electron microscopy. Here we report the isolation and
     characterization of the subfraction of the endoplasmic reticulum that is
     closely associated with the plasma membrane. This plasma membrane
     associated membrane (PAM) is characterized by its high capacity to
     synthesize phosphatidylserine and phosphatidylinositol. As such, PAM is
     reminiscent of MAM, a mitochondria associated membrane fraction of the
     yeast [Gaigg, B., Simbeni, R., Hrastnik, C., Paltauf, F. & Daum, G. (1995)
     Biochim. Biophys. Acta 1234, 214-220], although the specific activity of
     phosphatidylserine synthase and phosphatidylinositol synthase in PAM
     exceeds several-fold the activity in MAM and also in the bulk endoplasmic
     reticulum. In addition, several enzymes involved in ergosterol
     biosynthesis, namely squalene synthase (Erg9p),
     squalene epoxidase (Erg1p) and steroldelta24-methyltransferase (Erg6p),
     are highly enriched in PAM. A possible role of PAM in the supply of
     lipids to the plasma membrane is discussed.


=> d ibib abs 2-14

L80  ANSWER 2 OF 15  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER:   2002:220603  BIOSIS
DOCUMENT NUMBER:    PREV200200220603
TITLE:              Cytotoxicity of mevastatin and other cholesterol modulators
                    in acute myeloid leukemia.
AUTHOR(S):          Li, Henry Y. [Reprint author]; Stirewalt, Derek L. [Reprint
                    author]; Willman, Cheryl L.; Appelbaum, Frederick R.
                    [Reprint author]; Zager, Richard A. [Reprint author];
                    Banker, Deborah E. [Reprint author]
CORPORATE SOURCE:   Clinical Research Division, Fred Hutchinson Cancer Research
                    Center, Seattle, WA, USA
SOURCE:             Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp.
                    714a. print.
```

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002

AB The mevalonate biochemical pathway produces many substances necessary for cell viability, including sterols essential for membrane structure and steroid synthesis, ubiquinones needed for mitochondrial electron transport, retinoids involved in cell differentiation, and isoprenoids vital to the function of many membrane proteins. 3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase is the first rate-limiting enzyme in the mevalonate pathway, and since cholesterol is a product of this pathway, HMG-CoA reductase inhibitors (statins) are now widely used to treat hypercholesterolemia. Statins have also been shown to be selectively toxic to some tumors, including acute myeloid leukemia (AML). This toxicity has generally been attributed to their inhibition of isoprenoid production and the consequent inability of cells to prenylate proteins such as Ras and Rho. Using mevastatin as a prototypical statin, we examined the potential role of ras mutations in statin sensitivity by performing single-strand DNA conformation polymorphism analyses to interrogate both AML cell lines and primary AML cells for "hotspot" K-ras and N-ras mutations and by using Western blot assays to assess Ras protein characteristics. We found, however, that although mevastatin did reduce Ras protein modification and membrane localization in statin-sensitive AML cell lines with activating ras mutations, statin-sensitive primary AML cells did not necessarily carry ras mutations or over-express Ras protein. These cells also did not consistently demonstrate G1 cell cycle arrests or show the cyclin E and p27 responses associated with Rho inhibition in other statin models. In prior studies, though, we have shown that renal tubule cells increase membrane cholesterol pools in response to hypoxic and oxidant injuries and that mevastatin can sensitize these cells to injury. To determine whether cholesterol responses are similarly protective in AML and whether cholesterol reduction could contribute to the selective toxicity of statins in AML, we treated AML cell lines (HL60, KG1a, NB4, ML1) with mevastatin, zaragozic acid (an inhibitor of **squalene synthase**, the mevalonate pathway enzyme regulating cholesterol, but not isoprenoid, synthesis), or cholesterol modulators that chemically modify membrane cholesterol (including cholesterol oxidase, methylcyclodextrin, and cholesterol esterase). These treatments decreased cell cholesterol content by as much as 48%, as measured by gas chromatography and a **fluorescent** enzymatic assay. They were all toxic in AML cells as well, with NB4 cells demonstrating the highest sensitivity. This suggests that cholesterol reduction per se can kill AML cells. In addition, we found that cell cholesterol content rose markedly after exposure of AML cells to radiation or chemotherapy (cytarabine and daunorubicin), suggesting that cholesterol up-regulation is a stress response; the largest increase (>100%) occurred in the most statin-sensitive cell line (NB4). Co-treatment of these cells with cytarabine and either mevastatin or zaragozic acid resulted in apparently supra-additive toxicity, suggesting sensitization of cells to chemotherapy. Since zaragozic acid does not affect isoprenoid synthesis, these data suggest that cholesterol modulation may be one of the mechanisms by which mevastatin exerts its toxic effects on AML cells and that other cholesterol modulators may improve therapeutic ratios in AML by directly affecting cholesterol-dependent cytoresistance.

L80 ANSWER 3 OF 15 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:475935 SCISEARCH
THE GENUINE ARTICLE: 557GG
TITLE: Biosynthesis of secondary metabolites in sugarcane
AUTHOR: Franca S C (Reprint); Roberto P G; Marins M A; Puga R D; Rodrigues A; Pereira J O
CORPORATE SOURCE: Univ Ribeirao Preto UNAERP, Unidade Biotechnol Vegetal, Av Costabile Romano 2201, BR-14096380 Ribeirao Preto, SP, Brazil (Reprint); Univ Ribeirao Preto UNAERP, Unidade Biotechnol Vegetal, BR-14096380 Ribeirao Preto, SP, Brazil; Univ Amazonas, Fac Ciencias Agr, Manaus, Amazonas,

Brazil
COUNTRY OF AUTHOR: Brazil
SOURCE: GENETICS AND MOLECULAR BIOLOGY, (APR 2001) Vol. 24, No. 1-4, pp. 243-250.
Publisher: SOC BRASIL GENETICA, RUA CAP ADELMIO NORBET DA SILVA, 736, ALTO DA BOA VISTA, 14025-670 RIBEIRAO PRET, BRAZIL.
ISSN: 1415-4757.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A set of genes related to secondary metabolism was extracted from the sugarcane expressed sequence tag (SUCEST) database and was used to investigate both the gene expression pattern of key enzymes regulating the main biosynthetic secondary metabolism pathways and the major classes of metabolites involved in the response of sugarcane to environmental and developmental cues. The SUCEST database was constructed with tissues in different physiological conditions which had been collected under varied situation of environmental stress. This database allows researchers to identify and characterize the expressed genes of a wide range of putative enzymes able to catalyze steps in the phenylpropanoid, isoprenoid and other pathways of the special metabolic mechanisms involved in the response of sugarcane to environmental changes. Our results show that sugarcane cDNAs encoded putative ultra-violet induced sesquiterpene cyclases (SC); chalcone synthase (CHS), the first enzyme in the pathway branch for flavonoid biosynthesis; isoflavone synthase (IFS), involved in plant defense and root nodulation; isoflavone reductase (IFR), a key enzyme in phenylpropanoid phytoalexin biosynthesis; and caffeic acid-O-methyltransferase, a key enzyme in the biosynthesis of lignin cell wall precursors. High levels of CHS transcripts from plantlets infected with Herbaspirillum rubri or Gluconacetobacter diazotroficans suggests that agents of biotic stress can elicit flavonoid biosynthesis in sugarcane. From this data we have predicted the profile of isoprenoid and phenylpropanoid metabolism in sugarcane and pointed the branches of secondary metabolism activated during tissue-specific stages of development and the adaptive response of sugarcane to agents of biotic and abiotic stress, although our assignment of enzyme function should be confirmed by careful biochemical and genetic supporting evidence.

L80 ANSWER 4 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998382432 EMBASE
TITLE: H-Ras peptide and protein substrates bind protein farnesyltransferase as an ionized thiolate.
AUTHOR: Hightower K.E.; Huang C.-C.; Casey P.J.; Fierke C.A.
CORPORATE SOURCE: C.A. Fierke, Department of Biochemistry, Box 3711, Duke University Medical Center, Durham, NC 27710, United States. fierke@biochem.duke.edu
SOURCE: Biochemistry, (3 Nov 1998) 37/44 (15555-15562).
Refs: 74
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The zinc metalloenzyme protein farnesyltransferase (FTase) catalyzes the alkylation of a cysteine residue of protein substrates with a 15 carbon farnesyl group. We have developed **fluorescence** assays to directly measure the affinity of the enzyme for peptide and protein (Ras) substrates. A peptide corresponding to the carboxyl terminus of H-Ras binds to FTase in the .mu.M range (K(D) = 4 .mu.M) at physiological pH; however, the peptide affinity is enhanced approximately 70-fold in a ternary complex with an enzyme-bound farnesyl diphosphate (FPP) analogue, indicating that the two substrates bind synergistically. The pH dependence of substrate binding was also investigated, and two ionizations were observed: for the ternary complex, the pK(a) values are 8.1, reflecting ionization of the thiol of the free peptide, and 6.4. The pH dependence of the ligand-metal charge-transfer band in the optical absorption spectra of a Co2+-substituted FTase ternary complex suggests that a metal-coordinated

thiol ionizes with a pK(a) of 6.3. These data indicate that metal coordination of the peptide sulfur with the zinc ion in FTase lowers the pK(a) of the thiol resulting in formation of a bound thiolate at physiological pH.

L80 ANSWER 5 OF 15 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998445385 MEDLINE
DOCUMENT NUMBER: 98445385 PubMed ID: 9770500
TITLE: A novel amplicon at 8p22-23 results in overexpression of cathepsin B in esophageal adenocarcinoma.
AUTHOR: Hughes S J; Glover T W; Zhu X X; Kuick R; Thoraval D; Orringer M B; Beer D G; Hanash S
CORPORATE SOURCE: Department of Surgery, Section of Thoracic Surgery, University of Michigan Medical School, Ann Arbor, MI 48109, USA.
CONTRACT NUMBER: CA09672-06 (NCI)
CA26803 (NCI)
CA71606 (NCI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Oct 13) 95 (21) 12410-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981112

AB Cathepsin B (CTSB) is overexpressed in tumors of the lung, prostate, colon, breast, and stomach. However, evidence of primary genomic alterations in the CTSB gene during tumor initiation or progression has been lacking. We have found a novel amplicon at 8p22-23 that results in CTSB overexpression in esophageal adenocarcinoma. Amplified genomic NotI-HinfI fragments were identified by two-dimensional DNA electrophoresis. Two amplified fragments (D4 and D5) were cloned and yielded unique sequences. Using bacterial artificial chromosome clones containing either D4 or D5, **fluorescent** in situ hybridization defined a single region of amplification involving chromosome bands 8p22-23. We investigated the candidate cancer-related gene CTSB, and potential coamplified genes from this region including **farnesyl-diphosphate farnesyltransferase** (FDFT1), arylamine N-acetyltransferase (NAT-1), lipoprotein lipase (LPL), and an uncharacterized expressed sequence tag (D8S503). Southern blot analysis of 66 esophageal adenocarcinomas demonstrated only CTSB and FDFT1 were consistently amplified in eight (12.1%) of the tumors. Neither NAT-1 nor LPL were amplified. Northern blot analysis showed overexpression of CTSB and FDFT1 mRNA in all six of the amplified esophageal adenocarcinomas analyzed. CTSB mRNA overexpression also was present in two of six nonamplified tumors analyzed. However, FDFT1 mRNA overexpression without amplification was not observed. Western blot analysis confirmed CTSB protein overexpression in tumor specimens with CTSB mRNA overexpression compared with either normal controls or tumors without mRNA overexpression. Abundant extracellular expression of CTSB protein was found in 29 of 40 (72. 5%) of esophageal adenocarcinoma specimens by using immunohistochemical analysis. The finding of an amplicon at 8p22-23 resulting in CTSB gene amplification and overexpression supports an important role for CTSB in esophageal adenocarcinoma and possibly in other tumors.

L80 ANSWER 6 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998143794 EMBASE
TITLE: Photoaffinity labeling of oxidosqualene cyclase and squalene cyclase by a benzophenone-containing inhibitor.
AUTHOR: Abe I.; Yi Feng Zheng; Prestwich G.D.
CORPORATE SOURCE: Dr. G.D. Prestwich, Department of Medicinal Chemistry, University of Utah, 30 South, 2000 East, Salt Lake City, UT 84112-5820, United States. gprestwich@deans.pharm.utah.edu
SOURCE: Biochemistry, (28 Apr 1998) 37/17 (5779-5784).
Refs: 35

ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A new orally active oxidosqualene:lanosterol cyclase (OSLC) inhibitor (Ro48-8071; Morand, O. H. et al. (1997) J. Lipid Res. 38, 373-390) showed potent noncompetitive inhibition of bacterial squalene:hopene cyclase (SHC) from Alicyclobacillus acidocaldarius (IC50 = 9.0 nM, K(I) = 6.6 nM) and OSLC (IC50 = 40 nM, K(I) = 22 nM for homogeneous rat liver OSLC). A tritium-labeled isotopomer (18.8 Ci/mmol) of this nonterpenoid inhibitor, which possesses a benzophenone (BP) photophore, was chemically synthesized as a photoaffinity label. Specific, efficient covalent modification of both OSLC and SHC enzymes was observed after **UV** irradiation at 360 nm. Labeling of both OSLC and SHC by [3H]Ro48-8071 was competitively displaced by coincubation with a 1000-fold molar excess of 18-thia-2,3-oxidosqualene or the nonterpenoid inhibitor BIBX79. Displacement of labeling of OSLC was also achieved with the suicide substrate (3S)-29-methylidene-2,3-oxidosqualene. Thus, the nonsubstrate Ro488071 and both terpenoid and nonterpenoid inhibitors of these enzymes appear to share a common binding site.

L80 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:245899 CAPLUS
DOCUMENT NUMBER: 126:325304
TITLE: Farnesol-derived dicarboxylic acids in the urine of animals treated with zaragozic acid A or with farnesol
AUTHOR(S): Bostedor, Richard G.; Karkas, John D.; Arison, Byron H.; Bansal, Vinay S.; Vaidya, Sanskruti; Germershausen, John I.; Kurtz, Marc M.; Bergstrom, James D.
CORPORATE SOURCE: Merck Research Laboratories, Department of Biochemistry, Rahway, NJ, 07065-0900, USA
SOURCE: Journal of Biological Chemistry (1997), 272(14), 9197-9203
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Farnesyl diphosphate, the substrate for **squalene synthase**, accumulates in the presence of zaragozic acid A, a **squalene synthase** inhibitor. A possible metabolic fate for farnesyl diphosphate is its conversion to farnesol, then to farnesoic acid, and finally to farnesol-derived dicarboxylic acids (FDDCAs) which would then be excreted in the urine. Seven dicarboxylic acids were isolated by high performance liq. chromatog. (HPLC) from urine of either rats or dogs treated with zaragozic acid A or rats fed farnesol. Their structures were detd. by NMR anal. Two 12-carbon, four 10-carbon, and one 7-carbon FDDCA were identified. The profile of urinary dicarboxylic acids from rats fed farnesol was virtually identical to that produced by treating with zaragozic acid A, establishing that these dicarboxylic acids are farnesol-derived. By feeding [1-14C]farnesol and comparing the mass of the dicarboxylic acids produced with the **UV** absorption of the HPLC peaks, a method to quantitate the **UV**-absorbing FDDCAs was devised. When rats were treated with zaragozic acid A, large amts. of FDDCAs were excreted in the urine. The high level of FDDCAs that were found suggests that their synthesis is the major metabolic fate for carbon diverted from cholesterol synthesis by a **squalene synthase** inhibitor. A metabolic pathway is proposed to explain the prodn. of each of these FDDCAs.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:672934 CAPLUS
DOCUMENT NUMBER: 125:317306
TITLE: Methods for drug screening based on modeling transcriptional responsiveness of an organism to a candidate drug

INVENTOR(S): Ashby, Matthew; Rine, Jasper
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5569588	A	19961029	US 1995-512811	19950809
CA 2202154	AA	19970220	CA 1996-2202154	19960809
WO 9706277	A1	19970220	WO 1996-US12956	19960809
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9667209	A1	19970305	AU 1996-67209	19960809
AU 724474	B2	20000921		
EP 791078	A1	19970827	EP 1996-927362	19960809
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10507647	T2	19980728	JP 1996-508671	19960809

PRIORITY APPLN. INFO.: US 1995-512811 A 19950809
WO 1996-US12956 W 19960809

AB Methods and compns. for modeling the transcriptional responsiveness of an organism to a candidate drug involve (a) detecting reporter gene product signals from each of a plurality of different, sep. isolated cells of a target organism, wherein each cell contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional regulatory element of the target organism such that the transcriptional regulatory element regulates the expression of the reporter gene, and the sum of the cells comprises an ensemble of the transcriptional regulatory elements of the organism sufficient to model the transcriptional responsiveness of said organism to a drug; (b) contacting each cell with a candidate drug; (c) detecting reporter gene product signals from each cell; (d) comparing reporter gene product signals from each cell before and after contacting the cell with the candidate drug to obtain a drug response profile which provides a model of the transcriptional responsiveness of said organism to the candidate drug.

L80 ANSWER 9 OF 15 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:546954 SCISEARCH
THE GENUINE ARTICLE: UX165
TITLE: ANALYSIS OF ISOPRENOID PHOSPHATES AND OLIGOPHOSPHATES BY CAPILLARY ZONE ELECTROPHORESIS
AUTHOR: KELLER R K (Reprint); BANGALORE P; ROBERT J; SWANSON M G
CORPORATE SOURCE: UNIV S FLORIDA, COLL MED, DEPT BIOCHEM & MOLEC BIOL, 12901 N 30TH ST, TAMPA, FL, 33612 (Reprint); UNIV S FLORIDA, DEPT CHEM, TAMPA, FL, 33612
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CHROMATOGRAPHY A, (21 JUN 1996) Vol. 737, No. 2, pp. 325-331.
ISSN: 0021-9673.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 17

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

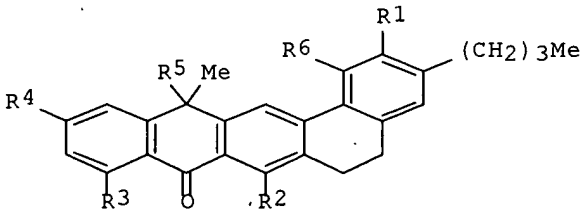
AB Capillary zone electrophoresis (CZE) has been used for the first time to analyse water-soluble phosphorylated isoprenoids, key intermediates in the branched pathway of mevalonate metabolism. Following synthesis, isoprenoid phosphates and oligophosphates were isolated by flash chromatography and their purity was established using P-31 NMR spectrometry. In developing optimum conditions for CZE, several factors were considered: ionization properties of the solutes, stability of the solutes and maximum signal-to-noise ratio. At pH 8.5 in 0.3 M sodium

berate buffer and monitoring **UV** absorbance at 200 nm, detection of farnesyl diphosphate was linear in the sub-picomol range; the limit of detection was ca. 12 fmol. For a given phosphorylated series (i.e., monophosphates, diphosphates, triphosphates), CZE cleanly resolved isoprenes of different chain length, and plots of relative mobility vs. M(r) were curvlinear. Remarkably, neryl phosphate (C10, alpha-cis-isoprene), geranyl phosphate (C10, alpha-trans-isoprene) and citronellyl phosphate (C10, alpha-saturated isoprene) were resolved. In addition, isopentenyl monophosphate (C5,Delta(3)) and dimethylallyl phosphate (C5,Delta(2)) exhibited different electrophoretic mobilities. These studies pave the way for future work on determining levels of phosphorylated isoprenoids in various tissues under conditions of altered mevalonate production.

L80 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:113257 CAPLUS
DOCUMENT NUMBER: 124:175626
TITLE: Preparation and formulation of anthracenone derivatives as antitumor agents and **squalene synthetase** inhibitors
INVENTOR(S): Shintani, Yasushi; Funahashi, Yasunori; Tozawa, Ryuichi
PATENT ASSIGNEE(S): Takeda Chemical Industries Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 23 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07258153	A2	19951009	JP 1994-53908	19940324

PRIORITY APPLN. INFO.: JP 1994-53908 19940324
OTHER SOURCE(S): MARPAT 124:175626
GI



I

AB The title compds. I [R1 = (esterified or amidated) carboxy; R2 - R6 = (etherified or esterified) OH] are claimed. I [R1 = CO2H; R2 = R3 = R4 = R6 = OH; R5 = MeO] (II) was isolated from culture medium of Streptomyces roseogriseus. The structure of II was detd. using 13C NMR, IR, and **UV** data. II in vitro showed IC50 of 7.5 .mu.g/mL against HeLa cells.

L80 ANSWER 11 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95116799 EMBASE
DOCUMENT NUMBER: 1995116799
TITLE: Brefeldin A renders Chinese hamster ovary cells insensitive to transcriptional suppression by 25-hydroxycholesterol.
AUTHOR: Ridgway N.D.; Lagace T.A.
CORPORATE SOURCE: Dept. of Pediatrics and Biochemistry, Atlantic Research Center, Dalhousie University, 5849 University Ave.,Halifax, NS B3H 4H7, Canada
SOURCE: Journal of Biological Chemistry, (1995) 270/14 (8023-8031). ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The effect of disruption of the Golgi apparatus on 25-hydroxycholesterol-mediated transcriptional suppression and activation of acyl-CoA:cholesterol acyltransferase was examined. In Chinese hamster ovary (CHO) cells, brefeldin A (BFA) caused dose-dependent inhibition of 25-hydroxycholesterol-mediated suppression of mRNAs for four sterol-regulated genes: 3-hydroxy-3- methylglutaryl (HMG)-CoA reductase, HMG-CoA synthase, farnesyl-diphosphate synthase, and the low density lipoprotein receptor. BFA prevented suppression whether added prior to or following a 4-h pretreatment with 25- hydroxycholesterol. In the presence of BFA (1 .mu.g/ml), 25-hydroxycholesterol- mediated suppression of mRNAs for HMG-CoA reductase, the low density lipoprotein receptor, and farnesyl-diphosphate synthase was almost completely blocked. HMG-CoA synthase nRNA was 80-90% suppressed by 25-hydroxy- cholesterol compared with 50-60% suppression in the presence of BFA. These effects of BFA were not due to alterations in mRNA stability. Disruption of the Golgi apparatus, as assessed by staining with a **fluorescent** lectin, correlated with concentrations of BFA that reversed mRNA suppression. Monensin was also found to block the effects of 25-hydroxycholesterol on suppression of HMG-CoA reductase. However, this ionophore decreased the other three sterol-regulated mRNAs to a similar degree as 25-hydroxycholesterol. In contrast to CHO cells, BFA-resistant PtK1 cells displayed normal down- regulation of HMG-CoA reductase and an intact Golgi apparatus in the presence of BFA and 25-hydroxy-cholesterol. Cholesterol esterification in CHO cells was stimulated to a similar extent by BFA (1 .mu.g/ml) and 25- hydroxycholesterol, and simultaneous treatment of CHO cells with both compounds was 60-70% additive. These results suggest that an intact Golgi apparatus is required for 25-hydroxycholesterol-mediated suppression of mRNA.

L80 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:692798 CAPLUS
DOCUMENT NUMBER: 121:292798
TITLE: Zaragozic??? acid derivatives as cholesterol-lowering compounds
INVENTOR(S): Treiber, Laszlo R.; Doss, George A.; Arison, Byron H.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 18 pp. Cont.-in-part of U.S. Ser. No. 963,142, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5322855	A	19940621	US 1992-980900	19921124
WO 9408575	A1	19940428	WO 1993-US9887	19931018
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9453614	A1	19940509	AU 1994-53614	19931018

PRIORITY APPLN. INFO.: US 1992-963142 19921019
US 1992-980900 19921124
WO 1993-US9887 19931018
OTHER SOURCE(S): MARPAT 121:292798

AB Zaragozic acids isolated from a culture of MF5453 are subjected to photoreaction, then derivatized at the 4-keto position. The resulting derivs. are active as **squalene synthetase** inhibitors and are useful in the treatment of hypercholesterolemia. A soln. of zaragozic acid A obtained from culture MF5453 was placed under a **fluorescent** light and reduced to give L-740,790.

L80 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:525261 CAPLUS
DOCUMENT NUMBER: 121:125261
TITLE: Zaragozic acid derivatives as cholesterol-lowering compounds
INVENTOR(S): MacConnell, John G.; Arison, Byron H.; Doss, George A.; Monaghan, Richard L.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 963,153, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5317031	A	19940531	US 1992-982163	19921124
WO 9407485	A1	19940414	WO 1993-US9144	19930927
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9351409	A1	19940426	AU 1993-51409	19930927

PRIORITY APPLN. INFO.:

US 1992-963153	B2	19921019
US 1992-957350	A	19921006
US 1992-979559	A	19921120
US 1992-982163	A2	19921124
WO 1993-US9144	W	19930927

OTHER SOURCE(S): MARPAT 121:125261

AB Cholesterol-lowering compds. and compns. are prepd. by the photochem. treatment of zaragozic acids followed by esterification. These compds. and compn. are active **squalene synthetase** inhibitors useful in the treatment of hypercholesterolemia. For example, zaragozic acid A isolated from a fungal ext. was treated with a **fluorescent** light and esterified. The intrinsic **squalene synthetase** inhibitory activity of the product was measured by the std. in vitro protocols.

L80 ANSWER 14 OF 15 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 94292167 MEDLINE
DOCUMENT NUMBER: 94292167 PubMed ID: 8020937
TITLE: Localization of the **squalene synthase** gene (FDFT1) to human chromosome 8p22-p23.1.
AUTHOR: Schechter I; Conrad D G; Hart I; Berger R C; McKenzie T L; Bleskan J; Patterson D
CORPORATE SOURCE: Eleanor Roosevelt Institute, Denver, Colorado 80206.
CONTRACT NUMBER: AG00029 (NIA)
SOURCE: GENOMICS, (1994 Mar 1) 20 (1) 116-8.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940815
Last Updated on STN: 19940815
Entered Medline: 19940729

AB Recently, we reported the isolation of a cDNA encoding the human enzyme **squalene synthase**, the first step of sterol biosynthesis uniquely committed to synthesis of cholesterol (6). As such, it is likely that this enzyme occupies a critical regulatory position in the synthesis of cholesterol. As part of continuing studies of the role of this gene in cellular metabolism, we undertook the mapping of this gene on the human chromosomes. To localize the gene, we have first isolated a yeast artificial chromosome (YAC) containing the **squalene synthase** gene. We then used **fluorescence** in situ hybridization (FISH) with yeast DNA containing the YAC to localize the gene to chromosome 8. Assignment to human chromosome 8 was confirmed by polymerase chain reaction analysis of a somatic cell hybrid containing

human chromosome 8. Use of a somatic cell hybrid regional mapping panel dividing chromosome 8 into several fragments localized the gene to 8p21-pter. Fractional length analysis of the FISH mapping placed the signal generated with this YAC at 8p22-p23.1.

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=> s NADPH and (fluorescen? or uv) and assay
L81        203 FILE MEDLINE
L82        232 FILE CAPLUS
L83        126 FILE SCISEARCH
L84         32 FILE LIFESCI
L85        174 FILE BIOSIS
L86        135 FILE EMBASE

TOTAL FOR ALL FILES
L87        902 NADPH AND (FLUORESCEN? OR UV) AND ASSAY

=> s NADPH and fluorescen and assay
L88          3 FILE MEDLINE
L89          6 FILE CAPLUS
L90          3 FILE SCISEARCH
L91          1 FILE LIFESCI
L92          2 FILE BIOSIS
L93          0 FILE EMBASE

TOTAL FOR ALL FILES
L94         15 NADPH AND FLUORESCEN AND ASSAY

=> dup rem l94
PROCESSING COMPLETED FOR L94
L95          11 DUP REM L94 (4 DUPLICATES REMOVED)

=> d ibib abs 1-11

L95  ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2001:417183  CAPLUS
DOCUMENT NUMBER:          135:30977
TITLE:                    Methods and compositions for detecting nitroaromatic
                          compounds by colorimetric assay using
                          xenobiotic reductase enzymes
INVENTOR(S):              Chambliss, Glenn H.; Fox, Brian G.; Noguera, Daniel
                          R.; Blehert, David S.; Knoke, Kyle L.
PATENT ASSIGNEE(S):       Wisconsin Alumni Research Foundation, USA
SOURCE:                   PCT Int. Appl., 39 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001040504      A2   20010607       WO 2000-US40996  20000926
     WO 2001040504      A3   20020606
     WO 2001040504      C2   20021114
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ,
             DE, DK, DZ, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
             TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1999-156370P  P  19990927
AB   Nitroarom. compds. present in various sample materials may be easily and
     inexpensively detected in a colorimetric assay according to the
     present invention. The invention includes a method of detecting
     nitroarom. compds., comprising placing a sample contg. a nitroarom. compd.
     in the presence of a xenobiotic reductase enzyme and observing the
     formation of a colored product. The invention also includes xenobiotic
     reductase enzymes, DNA sequences that encode such enzymes and derivs.
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thereof. The invention also includes compns. and kits for performing the **assay**. Xenobiotic reductase B was purified from Pseudomonas **fluorescens** I-C. The purified product was used with **NADPH** to **assay** for picric acid. The reaction mixt. produced a dark yellow-orange color.

L95 ANSWER 2 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:83624 SCISEARCH
THE GENUINE ARTICLE: 393FX
TITLE: Essential PchG-dependent reduction in pyochelin biosynthesis of Pseudomonas aeruginosa
AUTHOR: Reimmann C (Reprint); Patel H M; Serino L; Barone M; Walsh C T; Haas D
CORPORATE SOURCE: Univ Lausanne, Lab Biol Microbienne, Batiment Biol, CH-1015 Lausanne, Switzerland (Reprint); Univ Lausanne, Lab Biol Microbienne, CH-1015 Lausanne, Switzerland; Harvard Univ, Sch Med, Dept Biol Chem & Mol Pharmacol, Boston, MA 02115 USA
COUNTRY OF AUTHOR: Switzerland; USA
SOURCE: JOURNAL OF BACTERIOLOGY, (FEB 2001) Vol. 183, No. 3, pp. 813-820.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0021-9193.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The biosynthetic genes pchDCBA and pchEF, which are known to be required for the formation of the siderophore pyochelin and its precursors salicylate and dihydroaeruginoate (Dha), are clustered with the pchR regulatory gene on the chromosome of Pseudomonas aeruginosa. The 4.6-kb region located downstream of the pchEF genes was found to contain three additional, contiguous genes, pchG, pchH, and pchI, probably forming a pchEFGHI operon, The deduced amino acid sequences of PchH and PchI are similar to those of ATP binding cassette transport proteins with an export function. PchG is a homolog of the Yersinia pestis and I: enterocolitica proteins YbtU and Irp3, which are involved in the biosynthesis of yersiniabactin. A null mutation in pchG abolished pyochelin formation, whereas mutations in pchH and pchI did not affect the amounts of salicylate, Dha, and pyochelin produced. The pyochelin biosynthetic genes were expressed from a vector promoter, uncoupling them from Fur-mediated repression by iron and PchR-dependent induction by pyochelin. In a P. aeruginosa mutant lacking the entire pyochelin biosynthetic gene cluster, the expressed pchDCBA and pchEFG genes mere sufficient for salicylate, Dha, and pyochelin production. Pyochelin formation was also obtained in the heterologous host Escherichia coli expressing pchDCBA and pchEFG together with the E. coli entD gene, which provides a phosphopantetheinyl transferase necessary for PchE and PchF activation. The PchG protein was purified and used in combination with PchD and phosphopantetheinylated PchE and PchF in vitro to produce pyochelin from salicylate, L-cysteine, ATP, **NADPH**, and S-adenosylmethionine. Based on this **assay**, a reductase function was attributed to PchG. In summary, this study completes the identification of the biosynthetic genes required for pyochelin formation from chorismate in P, aeruginosa.

L95 ANSWER 3 OF 11 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002198874 MEDLINE
DOCUMENT NUMBER: 21928357 PubMed ID: 11931390
TITLE: Functional analysis of a chromosomal arsenic resistance operon in Pseudomonas **fluorescens** strain MSP3.
AUTHOR: Prithivirajsingh S; Mishra S K; Mahadevan A
CORPORATE SOURCE: Department of Experimental Radiation Oncology, University of Texas-MD Anderson Cancer Center, Houston 77030, USA.. pssingh@mdanderson.org
SOURCE: MOLECULAR BIOLOGY REPORTS, (2001) 28 (2) 63-72.
Journal code: 0403234. ISSN: 0301-4851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020405
Last Updated on STN: 20020919
Entered Medline: 20020918

AB We reported earlier about the detection of a chromosomally located arsenic operon (arsRBC) in a gram-negative bacterium Pseudomonas **fluorescens** strain MSP3, which showed resistance to elevated levels of sodium arsenate and sodium arsenite. The genes for arsenic resistance were cloned into the HindIII site of pBluescript vector producing three clones MSA1, MSA2 and MSI3 conferring resistance to sodium arsenate and arsenite salts. They were further sub-cloned to delineate the insert size and the sub-clones were designated as MSA11, MSA12 and MSI13. The sub-clone pMSA12 (2.6 kb) fragment was further packaged into EcoRI-PstI site of M13mp19 and sequenced. Nucleotide sequencing revealed the presence of three open reading frames homologous to the arsR, arsB and arsC genes of arsenic resistance. Three cistrons of the ars operon encoded polypeptides ArsR, ArsB and ArsC with molecular weights ranging approximately 12, 37and 24 kDa, respectively. These polypeptides were visualized on SDS-PAGE stained with Coomassie blue and measured in a densitometer. The arsenic resistance operon (arsRBC) of strain MSP3 plasmid pMSA12 consists of 3 genes namely, arsR--encoding a repressor regulatory protein, arsB--the determinant of the membrane efflux protein that confers resistance by pumping arsenic from the cells and arsC--a small cytoplasmic polypeptide required for arsenate resistance only, not for arsenite resistance. ArsB protein is believed to use the cell membrane potential to drive the efflux of intracellular arsenite ions. ArsC encodes for the enzyme arsenate reductase which reduces intracellular As(V) (arsenate) to more toxic As(III) (arsenite) and is subsequently extruded from the cell. The arsenate reductase activity was present in the soluble cytoplasmic fraction in E. coli clones. In the context of specified function of the arsenic operon encoded proteins, uptake and efflux mechanisms were studied in the wild strain and the arsenate/arsenite clones. The cell free filtrates of the arsenate clones (MSA11 and MSA12) obtained from P. **fluorescens** containing the arsC gene showed that arsenate reduction requires glutathione reductase, glutathione (GSH), glutaredoxin and ArsC protein. The protein was purified in an active form and a spectrophotometric **assay** was developed in which the oxidation of **NADPH** was coupled to reduction of arsenate. The molecular weights and the location of the polypeptides were obtained from Coomassie stained SDS-PAGE of extracellular and intracellular fractions of the cells.

L95 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:293605 CAPLUS
DOCUMENT NUMBER: 128:318804
TITLE: Enzymic cofactor cycling using soluble pyridine nucleotide transhydrogenase cloned from Pseudomonas **fluorescens**
INVENTOR(S): Bruce, Neil Charles; French, Christopher Edward
PATENT ASSIGNEE(S): Cambridge University Technical Services Ltd., UK; Bruce, Neil Charles; French, Christopher Edward
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818909	A1	19980507	WO 1997-GB2983	19971029
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747888	A1	19980522	AU 1997-47888	19971029
AU 709463	B2	19990826		

EP 939799 A1 19990908 EP 1997-910540 19971029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001502910 T2 20010306 JP 1998-520205 19971029
US 6440688 B1 20020827 US 1999-297468 19990712
PRIORITY APPLN. INFO.: GB 1996-22516 A 19961029
WO 1997-GB2983 W 19971029

AB In an enzymic reaction involving a pyridine nucleotide cofactor, an enzyme is used capable of transferring reducing equiv. between pyridine nucleotide cofactors. The gene (designated sth) encoding the sol. pyridine nucleotide transhydrogenase of Pseudomonas **fluorescens** NCIMB 9815 was cloned and sequenced, and the enzyme was overexpressed in Escherichia coli for the relatively easy prepn. of large amts. of enzyme. This enzyme catalyzed transfer of reducing equiv. between NAD and NADP, and is used so as to enhance a biotransformation process. It can also be used in enzyme-based anal. **assays** to convert a signal measured as oxidn. of **NADPH** to NADP to a signal that can be measured based on oxidn. of NADH to NAD. A specific example is the use of transhydrogenase in the **assay** of morphine in a morphine dehydrogenase/morphinone reductase system, such that redn. of hydromorphone is greatly decreased by avoiding accumulation of NADH. Alternatively, a cell transformed to express the enzyme may be used.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 5 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:105717 SCISEARCH
THE GENUINE ARTICLE: KM282
TITLE: PROPERTIES OF NADH **NADPH**-DEPENDENT P-HYDROXYBENZOATE HYDROXYLASE FROM MORAXELLA SP
AUTHOR: STERJIADES R (Reprint)
CORPORATE SOURCE: UNIV JOSEPH FOURIER, CTR ETUDES & RECH MACROMOLEC ORGANISES, BIOCHIM MICROORGANISMES LAB, F-38041 GRENOBLE, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: BIOTECHNOLOGY AND APPLIED BIOCHEMISTRY, (FEB 1993) Vol. 17, Part 1, pp. 77-90.
ISSN: 0885-4513.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The biodegradation of p-hydroxybenzoate by Moraxella sp., strain GU2, involves the initial conversion of the molecule into 3,4-dihydroxybenzoate by p-hydroxybenzoate hydroxylase. The enzyme is a flavoenzyme which can utilize either NADH or **NADPH** as an electron donor. The hydroxylase was purified to apparent homogeneity by the criteria of SDS/PAGE from p-hydroxybenzoate-induced cells of Moraxella sp. The apparent M(r) of the enzyme was determined to be 85 000 +/- 3 000 by Ultrogel AcA 44 gel filtration, and 45 000 +/- 1 000 by SDS/PAGE respectively, indicating that the enzyme consists of two polypeptide chains. On the basis of two-dimensional gel electrophoresis, the pI of the enzyme was estimated to be pH 6.55. The purified enzyme preparation contained 0.12 mol of FAD prosthetic group/mol of enzyme. Amino acid analysis shows that the enzyme contains relatively high amounts of acidic amino acids (21%) and hydrophobic amino acids (38%). No loss of enzyme activity was observed at 52-degrees-C for 20 min. In the presence of p-hydroxybenzoate (1 mM), the enzyme was stable at 60-degrees-C for 20 min. The enzyme was specific for p-hydroxybenzoate. No substrate-dependent oxidation of NADH was observed when substrate analogues of p-hydroxybenzoate, such as benzoate, p-nitrophenol, coumarate, p-hydroxybenzaldehyde, m-hydroxybenzoate, p-hydroxyphenylacetate and p-hydroxy-3-nitrobenzoate were used in the **assay**. High levels (2 mM) of either the substrate or substrate analogues inhibit enzyme activity. The apparent K(m) values for NADH and **NADPH** were 37 muM and 56 muM respectively.

L95 ANSWER 6 OF 11 MEDLINE on STN
ACCESSION NUMBER: 93049305 MEDLINE
DOCUMENT NUMBER: 93049305 PubMed ID: 1330553

TITLE: Ferrisiderophore reductases of Pseudomonas. Purification, properties and cellular location of the Pseudomonas aeruginosa ferripyoverdine reductase.
AUTHOR: Halle F; Meyer J M
CORPORATE SOURCE: Laboratoire de Microbiologie, Unite de Recherche Associee au Centre National de la Recherche Scientifique, no. 1481, Universite Louis Pasteur, Strasbourg, France.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1992 Oct 15) 209 (2) 613-20.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921203

AB Purification of the ferripyoverdine reductase from Pseudomonas aeruginosa, strain PAO1, lead to the isolation of a soluble protein of M(r) 27,000-28,000, as determined by HPLC sieving filtration and by denaturating gel electrophoresis. In the presence of NADH as the reductant, ferripyoverdine as the iron substrate, ferrozine as an iron(II)-trapping agent and FMN, this protein displayed an iron-reductase activity which resulted in the formation of ferrozine-iron(II) complex, providing that the enzymic **assay** was run under strict anaerobiosis. FMN was absolutely required for the activity to occur, but the lack of a visible spectrum and the lack of fluorescence for the protein in solution suggested that ferripyoverdine reductase is not a flavin-containing protein and that covalently bound FMN is not a prerequisite for the enzymatic reaction. A search of ferripyoverdine reductase by immunological detection amongst the different cellular compartments of P. aeruginosa lead to the conclusion that the soluble enzyme, which represented more than 95% of the total cellular enzyme, is not located in the periplasm but specifically in the cytoplasm. A strongly immunoreacting material, corresponding to a protein with identical M(r) as the ferripyoverdine reductase of P. aeruginosa PAO1, was detected in all the eighteen fluorescent pseudomonad strains belonging to the P. aeruginosa, P. **fluorescens**, P. putida and P. chlororaphis species, as well as in P. stutzeri, a non-fluorescent species, suggesting that the enzyme acting as a ferripyoverdine reductase in P. aeruginosa PAO1 is ubiquitous among the Pseudomonas.

L95 ANSWER 7 OF 11 MEDLINE on STN
ACCESSION NUMBER: 91264222 MEDLINE
DOCUMENT NUMBER: 91264222 PubMed ID: 1904691
TITLE: Adaptation of an enzymatic fluorescence **assay** for L-glutamic acid decarboxylase.
AUTHOR: Wolf R; Klemisch H
CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Munich, Federal Republic of Germany.
SOURCE: ANALYTICAL BIOCHEMISTRY, (1991 Jan) 192 (1) 78-81.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910802
Last Updated on STN: 19970203
Entered Medline: 19910718

AB The activity of L-glutamic acid decarboxylase (GAD) is commonly estimated by several radiometric methods, whereas a fluorimetric **assay** based on an enzymatic formation of **NADPH** as described by Y. Okada and C. Shimada [(1975) Brain Res. 98, 202-206] has been given little attention in biochemical and pharmacological investigations. A simple modification of this **assay** is presented to permit rapid and sensitive GAD measurements in unpurified tissue homogenates. This method, employing a linear **NADPH** standard curve, is demonstrated to be a valid **assay** system for a pharmacological approach using 3-mercaptopropionic acid.

L95 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:22290 BIOSIS
DOCUMENT NUMBER: PREV198120022290; BR20:22290
TITLE: GENERATION OF COLOR FROM PYRIDINE NUCLEOTIDES IN SOLUTION OR ON STRIPS.
AUTHOR(S): CAMERON E C [Reprint author]; WHITESTEVENS R H; GUNTER C R
CORPORATE SOURCE: AMES RES LAB, AMES CO, DIV MILES LAB INC, ELKHART, INDIANA 46515, USA
SOURCE: Clinical Chemistry, (1980) Vol. 26, No. 7, pp. 1057. Meeting Info.: JOINT MEETING OF THE AMERICAN ASSOCIATION FOR CLINICAL CHEMISTRY AND THE CANADIAN SOCIETY OF CLINICAL CHEMISTS, BOSTON, MASS., USA, JULY 20-25, 1980. CLIN CHEM. CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L95 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:633536 CAPLUS
DOCUMENT NUMBER: 93:233536
TITLE: A convenient **assay** for .gamma.-aminobutyric acid transaminase
AUTHOR(S): Rengachary, Setti S.; Yang, Bob In-Yu
CORPORATE SOURCE: Coll. Arts Sci., Univ. Missouri, Kansas City, MO, 64110, USA
SOURCE: Brain Research Bulletin (1980), 5(Suppl. 2), 51-5 CODEN: BRBUDU; ISSN: 0361-9230
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A facile technique is reported for sepg. succinate semialdehyde dehydrogenase (I) from .gamma.-aminobutyrate transaminase (II) in a com. available mixt. of the 2 enzymes. Isolated I was a suitable coupling enzyme for the spectrophotometric **assay** of II from various sources. To obtain I, the enzyme mixt. was 1st passed through a gel filtration column in 50 mM phosphate buffer, pH 7.2, to remove interfering ions. The filtrate was then adsorbed onto an affinity column of com. obtainable .beta.-NADP-agarose. II was removed with 50 mM phosphate buffer, pH 7.2. I was then specifically desorbed with 10 mM NADP in the same buffer. A 76% yield was obtained. Contamination by II and **NADPH** oxidase was 0.2 and 0.04%, resp. The enzyme so prepd. was stable, e.g. retaining up to 89% of its activity after 24 days, when stored in concd. form in the presence of glycerol plus bovine serum albumin or egg yolk lysolecithin. II activity detd. by the coupled spectrophotometric **assay** was compared to that obtained in a direct radioisotopic method.

L95 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:484423 CAPLUS
DOCUMENT NUMBER: 75:84423
TITLE: Anthranilic acid conversion to catechol (by Pseudomonas)
AUTHOR(S): Kobayashi, Shuhei; Hayaishi, Osamu
CORPORATE SOURCE: Inst. Virus Res., Kyoto Univ., Kyoto, Japan
SOURCE: Methods Enzymol. (1970), Volume 17, Issue Pt. A, 505-10. Editor(s): Colowick, Sidney P. Academic: New York, N. Y. CODEN: 18HWA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB P. **fluorescens**, No. 23 (ATCC 11,250) produces 2 unidentified sol. protein factors "enzyme A" (I) and "enzyme B" (II). Together, they convert anthranilate (III) to catechol. Neither I or II singly have such activity. The prepn., purification, and **assay** of I and II are described. Both NADH and **NADPH** activate I plus II against III. The enzyme system also reacts with 5- and 3-hydroxyanthranilic acids. Compared to the III reaction, the rates are 85% and 40%, resp. Purified I is unstable in air but II is stable. It can be preserved for >1 week at 4.degree. without detectable activity loss. The reaction of III with I and II is strongly inhibited by 10-5M p-chloromercuribenzoate or o-phenanthroline. Higher concns. of cyanide, azide, CO, and aminopterin

were not inhibitory. Fe2+ (10-4M) activates the reaction to a variable extent; however, other metallic ions, including Fe3+, Mn2+, and Mg2+ do not affect the reaction at that concn. The enzyme system has its max. activity at pH 7.3.

L95 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:43870 CAPLUS
DOCUMENT NUMBER: 66:43870
TITLE: Rapid screening **assays** for soluble and particulate bacterial dehydrogenases
AUTHOR(S): Kersters, K.
CORPORATE SOURCE: Fac. Sci., State Univ., Ghent, Belg.
SOURCE: Antonie van Leeuwenhoek (1967), 33(1), 63-72
CODEN: ALJMAO; ISSN: 0003-6072
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Assays** for sol. NAD- and NADP-linked dehydrogenases were described, based on the fluorescence of NADH and **NADPH**. The procedure detected <0.0003 micromole of NADH or **NADPH** and required only 15 min. for testing one bacterial ext. with 40 different substrates. One .mu.l. of each 0.4M substrate soln. was spotted on Whatman No. 1 filter paper which had been buffered by soaking in Tris-HCl buffer (0.2M, pH 8.0) contg. 0.001M MgCl2, and air dried. Such dry substrate papers were stable for at least 1 month when stored at -12.degree. in dry, well closed containers. For **assay** of a bacterial ext. contg. sol. dehydrogenases, 0.06 ml. of the ext. was mixed with 0.02 ml. of 0.025M NAD or NADP, and the mixt. was spotted on each dried substrate spot. The paper was immediately pressed between glass plates to prevent evapn. After 15 min., the paper was air-dried and examd. for fluorescence upon irradiation at 360 m.mu.. For **assay** of particulate dehydrogenases, the enzyme prepns. were suspended in phosphate buffer, 0.02M, pH 6.5. Substrate soln. (0.1 ml.) was added to 0.3 ml. of a soln. of 2,6-dichloroindophenol (0.00025M) in phosphate buffer (0.02M, pH 6.5). The enzyme soln. (0.1 ml.) was added and the degree of bleaching followed visually after 10, 30, and 60 min. at room temp. Exts. of Gluconobacter[Acetobacter] suboxydans contained sol. NADP-linked dehydrogenases for glucose, galactose, gluconate, glucitol, mannitol, and meso-ribitol. Wide differences were shown in the particulate dehydrogenase content of Pseudomonas **fluorescens**, P. putida, P. rubescens, A. suboxydans, and Escherichia coli.

=> s NADPH and uv and assay
TOTAL FOR ALL FILES
L102 172 NADPH AND UV AND ASSAY

=> s l102 and squalene
TOTAL FOR ALL FILES
L109 1 L102 AND SQUALENE

=> d ibib abs

L109 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:656318 CAPLUS
DOCUMENT NUMBER: 139:193613
TITLE: Fluorescent **assay** for **squalene** synthase amenable to high-throughput use, and cloning and expression of a truncated Arabidopsis **squalene** synthase
INVENTOR(S): Stevens, Donna; Wang, Xiao-zhuo; Rice, John; Nye, Beth; Broadwell, David; Glassbrook, Norman; Sevala, Veeresh; Crawford, John; Stewart, Sandy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003157583	A1	20030821	US 2001-24130	20011217

PRIORITY APPLN. INFO.: US 2001-24130 20011217

AB The cloning of a truncated Arabidopsis gene expressing **squalene** synthase, as well as the expression and purifn. of the **squalene** synthase, are described. Also described herein is a fluorescent **assay** using **squalene** synthase that is amenable to high-throughout use, particularly for studying the regulation of isoprenoid synthesis and identifying **squalene** synthase inhibitors and promoters. As the formation of **squalene** is stoichiometric with the depletion of **NADPH**, the activity of **squalene** synthase can be evaluated by following the **NADPH** concn. over time. **Squalene** synthase activity is detd. by combining FPP, **NADPH**, **squalene** synthase and a magnesium ion cofactor to form a reaction mixt. under conditions suitable for **squalene** formation, optionally in the presence of a compd. being analyzed for its ability to inhibit or promote **squalene** synthase. The concn. of **NADPH** over time is detd. by subjecting the reaction mixt. to **UV** light and detecting fluorescent light emission.

=> s l102 and farnesyl

TOTAL FOR ALL FILES
L116 1 L102 AND FARNESYL

=> log y